Reducing antibiotic prescribing in primary care in England from 2014 to 2017. Population-based cohort study

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Short title: Antibiotic utilisation in primary care

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ABSTRACT

Objective: This study aimed to analyse individual-patient electronic health records to evaluate changes in antibiotic (AB) prescribing in England for different age-groups, for males and females, and by prescribing indications from 2014 to 2017.

Methods: Data were analysed for 102 general practices in England that contributed data to the UK Clinical Practice Research Datalink (CPRD) from 2014 to 2017. Prescriptions for all ABs and for broad-spectrum β-lactam ABs were evaluated. Relative rate reductions (RRR) were estimated from a random effects Poisson model adjusting for age, gender and general practice.

Results: Total AB prescribing declined from 608 prescriptions per 1,000 person years in 2014 to 489 per 1,000 in 2017; RRR, 6.9% (95% confidence interval 6.6 to 7.1%) per year. Broad-spectrum β-lactam AB prescribing decreased from 221 per 1,000 in 2014 to 163 per 1,000 in 2017; RRR 9.3% (9.0% to 9.6%) per year. Declines in AB prescribing were similar for men and women but the rate of decline was lower over the age of 55 years than for younger patients. All AB prescribing declined by 9.8% (9.6% to 10.1%) per year for respiratory infections, 5.7% (5.2% to 6.2%) for genito-urinary infections but by 3.8% (3.1% to 4.5%). Overall, 38.8% of AB prescriptions were associated with codes that did not suggest specific clinical conditions and 15.3% of AB prescriptions had no medical codes recorded.

Conclusion: Antibiotic prescribing has reduced and become more selective but substantial unnecessary AB utilisation may persist. Improving the quality of diagnostic coding for AB utilisation will help to support antimicrobial stewardship efforts.

Key words: antibiotics; primary care; antimicrobial resistance; broad-spectrum β-lactam antibiotics; respiratory tract infection

Strengths and limitations of this study

- The study findings are derived from analysis of electronic health records data for more than 100 general practices in England that continuously contributed to CPRD data set over the study period.
- Comprehensive data for all antibiotic prescriptions and consultations at general practice surgeries were analysed.
- Antibiotic prescriptions issued outside general practices in out-of-hours settings were not captured.
- Antibiotic prescriptions may not always have been dispensed or taken by patients.

INTRODUCTION

Antimicrobial resistance (AMR) is a growing concern world-wide.(1, 2) Many disease-causing pathogens have now developed resistance to antimicrobial drugs. (3) The pathways to high rates of antibiotic resistance at population level are complex but excessive antibiotic utilisation in the context of medical care is often a proximal cause of antibiotic resistance (4, 5) especially in community settings.(6-8) Consequently, there are increasing calls for more carefully considered use of antibiotics in healthcare settings in order to conserve the therapeutic potential of available antimicrobial drugs.(9) This is particularly relevant in primary care settings where more than 70% of all antibiotics are prescribed. (10, 11) Inappropriate AB prescribing is known to be widespread in primary care.(12) Based on international comparisons, with both low- (13) and high-(14) antibiotic prescribing being observed across Europe, without comparable variation in safety outcomes such as bacterial infections, it appears that a substantial reduction of present antibiotic prescribing in primary care might be safe and feasible.

In order to address these concerns, aggregated data for antibiotic prescribing are now being used for health service management. A contractual financial incentive, known as a 'Quality Premium', has been introduced into the English NHS for meeting indicative targets for year-on-year reductions in inappropriate AB utilisation across all indications (15). The English Surveillance Programme for Antimicrobial Utilisation and Resistance (ESPAUR)(10) analysed aggregated prescribing data and found that general practice antibiotic prescriptions decreased by 13% between 2012 and 2016. Analysis of data for individual patients offers an opportunity for more detailed understanding of this decreasing trend. Dolk et al.(16) analysed data from the THIN database from 2013 to 2015 and drew attention to limitations of primary care records as a data source, including the high proportion of antibiotic prescriptions for which no 'clinical justification' was recorded. The purpose of the present study is to update data for antibiotic prescribing trends in English general practices from 2014 to 2017. The analyses specifically aimed to provide estimates for the decline in antibiotic use separately for males and females and for people of different ages. We also aimed to evaluate which prescribing indications, were most associated with reduced prescribing. We compared changes in all antibiotic prescribing with changes in prescribing of broad-spectrum beta-lactam antibiotics. Finally, we aimed to compare reductions in prescribing of individual major classes of antibiotics to provide complementary information.

METHODS

Data source

The UK Clinical Practice Research Datalink (CPRD) (17) was used as the data source for the study. This is a prospectively collected primary care database including data from approximately 7% of UK general practices. The total number of patients ever registered in CPRD is about 11 million, but the registered population has varied over time and by 2017 there were approximately 2.5 million active UK patients. In the UK, more than 98% of the population are registered with a general practice and registrations are often maintained over many years. The CPRD is considered to be representative of the UK population. (17) Data collected into CPRD are of high quality and include all medical diagnoses recorded at consultations and referrals, as well as all drug prescriptions issued by general practices. (18) For this study we included data from CPRD general practices in England, which participated in the data linkage scheme, and consistently contributed data in all years from 2014 to 2017. During this period the total number of general practices in the UK contributing to CPRD declined from 491 in 2014 to 285 in 2017. The number of CPRD general practices in England declined from 329 to 133, while the number participating in the data linkage scheme declined from 257 to 102. (Supplementary Table 1). Individual participant data were included from the later of 1st January 2014 or the start of the patient's CPRD record to the earlier of 31st December 2017 or the end of the patient's CPRD record. Data were obtained from the February 2018 release of CPRD. For practices that ended CPRD data collection during 2017, an equivalent end-of-year-date was also adopted for earlier years, because of the marked seasonality in antibiotic utilisation.

Main measures

For each year of study, we calculated the person-time contributed by each patient between 1st January of the year, or start of registration if this was later, to 31st December of the year, or end of registration or date of death, if these were earlier. Person-time was employed as denominator for rates. Prescriptions for antibiotics were identified using product codes for all antibiotic drug classes included in section 5.1 of the British National Formulary (BNF) except anti-tuberculous, anti-lepromatous agents and methenamine, which were excluded.(19) The BNF groups antibiotic drugs into the following categories: penicillins, cephalosporins (including carbapenems), tetracyclines, aminoglycosides, macrolides, clindamycin, sulphonamides (including combinations with trimethoprim), metronidazole and tinidazole, quinolones, drugs for urinary tract infection (nitrofurantoin) and other antibiotic drugs. We analysed broad-spectrum β-lactam antibiotics as a separate group, including the *British National Formulary* category of 'broad-spectrum penicillins' (19) and cephalosporins. The category of 'broad-spectrum penicillins' includes ampicillin and amoxycillin and combinations with clavulanic acid or flucloxacillin. Carbapenems, which are only rarely used in primary care, were combined with cephalosporins for these analyses. Clinical indications for antibiotic prescription were grouped into categories based on Read medical codes recorded into patients' clinical and referral records on the same date as the AB prescription including: 'respiratory conditions', 'genitourinary conditions', 'skin' conditions, 'eye' conditions, or no codes recorded. (Supplementary Table 2 to 5). All other codes were grouped into a single category of 'other and non-specific codes'. The most frequently used codes in this category are shown in Table 1 and included ‘telephone encounter’, ‘patient reviewed’ and ‘telephone triage encounter’ as the most frequently used codes. Since specific coded indications for antibiotic therapy were infrequent in this category, it is subsequently referred to as ‘non-specific’. We analysed the prescription sequence variable to determine whether each prescription was the first in a sequence or whether it was a repeat prescription; the former were coded as ‘acute’ prescriptions and the latter were coded as ‘repeat‘ prescriptions.

Statistical analysis

Antibiotic prescriptions for all AB and broad-spectrum β-lactam AB were enumerated by year. AB prescriptions of the same type on the same date were considered as a single event. Age was included as a continuous covariate but was also analysed in sub-groups from 0-4 years, then 10-year age-groups up to 85 years and over. Read codes recorded on the same date as an AB prescription were analysed according to indication. The primary indication on each date was allocated by giving priority to indications in the following sequence: respiratory, genitourinary, skin and eye. We estimated antibiotic prescription rates per 1,000 person years, and proportions of registered patients with AB prescribed in year in relation to age-group, gender, study year and main indication. In order to estimate annual changes in antibiotic prescribing, we fitted in hierarchical generalized linear Poisson models using the ‘hglm’ package (20) in the R program. The dependent variable was a count of antibiotic prescriptions (either all AB prescriptions or broad-spectrum β-lactam AB prescriptions). Predictors were calendar year, gender and age, including quadratic and cubic terms to allow for non-linear effects of age. Calendar year was included as a linear predictor based on inspection of descriptive data and because non-linear effects would be difficult to estimate over a four year period. A random effect for general practice was included because of the repeated observations on general practices over years. The log of person-time was included as offset. Relative rate reductions were estimated as one minus the adjusted relative rate for the linear effect of calendar year. In view of the size of the dataset, we present confidence intervals rather than significance tests. Results were presented using the ‘ggplot2’ and ‘forestplot’ packages (21) in the R program (22).

Research Ethics

The research protocol for this study was submitted to and approved by the Medicines and Healthcare Products Regulatory Agency (MHRA) Independent Scientific Advisory Committee (ISAC), Protocol 16_020. All patients’ electronic health records analysed for this study were fully anonymized.

Patient and Public involvement

Neither patients nor public were involved in the development and design of this study, nor the selection of outcome measures, nor the conduct, analysis and dissemination of the study.

RESULTS

Overall antibiotic prescriptions

Analyses included 102 general practices that contributed data in each year from 2014 to 2017 (Table 2). The registered population was 1.03 million in 2014 increasing to 1.07 in 2017. There were 539,219 AB prescriptions in 2014, declining to 459,476 in 2017. The AB prescribing rate declined from 608 per 1,000 in 2014 to 489 per 1,000 in 2017. The proportion of registered patients that were prescribed antibiotics in each year declined from just over 1 in 4 (25.3%) in 2014 to just over 1 in 5 (21.1%) in 2017. Figure 1 (left panel) shows changes in the proportion of patients prescribed antibiotics by year over the study period. A consistent year-on-year reduction was observed in each age-group from 0 to 4 years to 85 years and over. Marked antibiotic prescribing variations were observed in relation to age, with the highest rates at the extremes of age.

There were 195,750 broad-spectrum β-lactam AB prescriptions in 2014, declining to 153,423 in 2017. The proportion of all AB prescriptions that were broad-spectrum β-lactams decreased from 36.3% in 2014 to 33.3% in 2017 (Table 2). Figure 1 (right panel) shows the change in proportion of patients prescribed broad spectrum β-lactam AB by age-group. While there was a year-on-year decrease in broad-spectrum β-lactam AB use in each age-group, the absolute reduction appeared to be greater at older ages in whom broad-spectrum β-lactam AB use was greatest.

Table 3 presents data for AB prescribing indications. Respiratory consultations accounted for the most frequent defined indication with 168,852 (31%) prescriptions in 2014 and 129,032 (28%) in 2017. Genitourinary infections and skin infections accounted for 9% and 7% of AB prescriptions respectively with little change over years. There were 77,431 (14%) AB prescriptions with no associated medical codes recorded in 2014 and 73,596 (16%) in 2017. There were 204,395 (39%) of antibiotic prescriptions with other and non-specific codes recorded in 2014 and 181,018 (39%) in 2017. Overall, there were more than half (54.1%) of the AB prescriptions were documented without specific clinical conditions recorded.

Table 4 shows the proportion of repeat prescriptions for different prescribing indications. In 2017, 78,166 (17%) of antibiotic prescriptions were recorded as repeat prescriptions. The proportion of repeat prescriptions was 2% or lower for respiratory, genitourinary or eye conditions. For skin infections, 8% of antibiotic prescriptions were recorded as repeat prescriptions. There were 10% of repeat prescriptions among antibiotic prescribing episodes associated with non-specific codes. Among 73,596 antibiotic prescriptions in 2017 with no medical codes recorded, 56,216 (76%) were recorded as repeat prescriptions.

Informed by the apparent consistent annual declines in antibiotic prescribing noted in Table 2 and Figure 1, Figure 2 presents a Forest plot of annual relative reductions in AB prescribing adjusted for age, gender and general practice. Estimates for all antibiotic prescribing are shown in blue and for broad-spectrum β-lactam AB prescribing in red. The annual relative reduction in all AB prescribing was 6.9% (95% confidence interval 6.6% to 7.1%). Estimates were generally similar for males and females. For participants aged less than 55 years, the sub-group estimates were all greater than the overall estimate, being greatest at age 45 to 54 years at 9.2% (8.4% to 9.9%) per year. For participants older than 55 years, estimates were consistently lower than the overall estimate being lowest at age 75 to 84 years and above at 4.3% (3.4% to 5.1%) per year. Considering sub-groups of indications, rates of decline were greatest for respiratory indications (9.8%, 9.6% to 10.1%), and eye indications (11.0%, 9.9% to 12.2%). The rate of decline was smallest for AB prescriptions with no recorded indication (3.8%, 3.1% to 4.5%). The overall rate of decline was faster for broad-spectrum β-lactam AB than all AB at 9.3% (9.0% to 9.6%). Estimates were consistent for males and females. The greatest relative decline was observed at 45 to 54 years (12.5%, 11.5% to 13.5%) and the lowest at 75 to 84 years (5.7%, 4.7% to 6.7%). The greatest decline was for skin condition indications (14.9%, 13.9% to 15.9%) and lowest for un-coded indications (5.5%, 4.5% to 6.4%).

Changes in different classes of antibiotics

Figure 3 presents changes over time in the utilisation of different classes of antibiotics. The most frequently issued antibiotics were penicillins, accounting for 56% of AB prescriptions in men and 44% in women in 2017; macrolides, men 14%, women 12%; tetracyclines, men

14%, women 12%; sulphonamide and trimethoprim combination, men 6%, women 11%. the latter class be more frequently used in females. Clindamycin, aminoglycosides and other antibiotics accounted for less than 1% of antibiotic prescriptions and are not shown. During the period of study, drugs for urinary tract infections (nitrofurantoin) increased as a proportion of all antibiotic prescriptions, in men from 2.6% in 2014 to 4.2% in 2017, and in women from 8.8% in 2014 to 13.7% in 2017. Tetracycline use also increased between 2014 and 2017, in men from 12.8% to 14.5% and in women from 10.1% to 11.6%. Most other categories appeared to show slight declines. Both penicillin and macrolides were mainly prescribed for treating respiratory conditions, whereas tetracyclines was frequently issued for skin conditions among young patients and respiratory conditions in later life. There was a decline in the use of sulphonamide/trimethoprim combinations for urinary conditions while a notable increase of nitrofurantoin use for these conditions was observed over study years among all age groups but more particularly in women.

DISCUSSION

Main findings

The rate of antibiotic prescriptions and the proportion of patients receiving antibiotics have declined consistently over this four-year period. Antibiotic utilisation shows important patterning by age and gender, being higher in very young and very old people and higher in women than men. However, the present results show that a reduction in antibiotic utilisation is being achieved across all ages groups and in females as well as males. The gender gap in relation to antibiotic prescribing could be due to differences in medical care-seeking behaviour or specific conditions which disproportionally affect one gender (23). Among prescriptions associated with coded indications, respiratory conditions were the most frequent indication for antibiotic prescription and also showed the greatest rate of decline. Consistent with other recent reports,(16) we find that a substantial proportion of antibiotic prescriptions are not associated with specific coded clinical indications out of which a major share was associated with repeat prescriptions. Antibiotic prescriptions that were not associated with medical codes, showed the slowest rate of decline, potentially further identifying this category of prescriptions as representing a sub-optimal standard of clinical practice which might hamper the accurate estimation of drug indications. Therefore, enhancing the quality of clinical information recording is warranted in order to improve patient care, as well as the usefulness of records for research and health service management.

More than one third of prescriptions were for β-lactam antibiotics and there was evidence of an important decline in antibiotic prescribing in this category consistent with previous evidence. (10) The relative reductions of broad-spectrum β-lactam prescriptions were greater than for overall antibiotic utilisation. Broad-spectrum β-lactam antibiotics may not necessarily offer more effective coverage of causal pathogens than their more specific counterparts. The present results suggest that clinicians are gradually shifting to more targeted narrow-spectrum substitutions when possible. There is no universally accepted definition for ‘broad-spectrum’ antibiotics.(10, 19) This study analysed a separate category of β-lactam antibiotics that were broad-spectrum (as ‘broad-spectrum beta-lactam antibiotics’) to illustrate the possible difference in prescribing trends between these broad-spectrum antibiotics and their counterparts. For most common and uncomplicated infections, narrower spectrum drugs are generally recommended as first-line agents in general practices (24). Macrolides are generally recommended as substitutions for penicillin in the case of penicillin allergy, as well as for specific indications including Legionella or the eradication of Helicobacter pylori (HP). Nevertheless, macrolides were frequently prescribed in this and other studies. (25, 26). Clinical use of tetracyclines was low in children in recognition of the risk of deposition in growing bone and teeth (27) but the overall use of tetracyclines was higher at other ages. The increase of nitrofurantoin utilization was mainly due to the shift of guideline recommendation from trimethoprim to nitrofurantoin as empiric treatment for UTI (24).

Strengths and limitations

The study included more than 100 general practices in England that participated consistently across the four-year period of study. The CPRD includes general practices from throughout the UK. However, because the CPRD licence imposes limits on the size of dataset to be employed, we selected only CPRD general practices in England. During the period of the study, there was substantial attrition of the cohort of CPRD general practices as practices migrated from the Vision practice systems that was employed by practices contributing to the CPRD database. We considered that it was important to include the same general practices in each year of study, with more than 100 general practices included in total. However, we cannot be sure whether the antibiotic prescribing of general practices that left the CPRD might differ from those that remained. Previous studies have demonstrated the high quality and completeness of primary care electronic health records in CPRD.(17) The data suggested that repeat antibiotic prescriptions might account for a high proportion of uncoded prescriptions but the prescription sequence field has not been well-validated to our knowledge. A concern for the present study is the possible lack of recording of out-of-hours prescriptions, especially those from deputising services, walk-in centres and emergency care settings (28). We noted that codes for telephone consultations and home visits were frequent among antibiotic prescriptions with non-specific coded indications, which suggests that some out-of-hours activity may have been captured. We also acknowledge that prescriptions from hospitals and specialist clinics are not included, but these are expected to make only a small contribution to community antibiotic utilisation. It appears unlikely that the large and consistent reductions in prescribing observed in this paper could be accounted for by shifting of prescribing to other care settings. The research analysed prescriptions issued and not prescriptions dispensed or consumed by patients. We were not able to determine whether prescribers used a delayed or deferred antibiotic prescribing strategy. For these reasons, we believe that actual antibiotic consumption may be slightly lower than we have reported. We acknowledge that there are variations in prescribing between practices,(16, 29, 30) our analytical method allowed us to estimate overall effects, and measures of precision, that accommodated variation between practices. Our results show some difference from an earlier study(16) in terms of distribution of indications, but since different general practices, from different databases, were included in the two studies this may reflect variations in clinical practice.

Comparison with other studies

Previous analyses of primary care electronic health records have focused on antibiotic prescribing for respiratory infections,(31, 32) recognising that these conditions represent the most frequent indications for antibiotic prescription. There has been a long-term decline in respiratory consultation rates in England that has contributed to reducing antibiotic utilisation for these conditions.(31) Some authors suggest that respiratory consultations account for nearly two thirds of antibiotic utilisation in primary care.(33) Our analyses are consistent with those of Dolk et al.(16), who found that respiratory consultations account for fewer than half of antibiotic prescriptions. However, a high proportion of prescriptions may be associated either with no medical codes or non-specific codes making interpretation difficult. There were further methodological differences between the Dolk et al.(16) study and our own, the former study relied on the THIN database with a different number of general practices participating in different years, as well as using code lists that may have differed in some respects. Consequently, minor numerical differences are to be expected.

Conclusions

The present analyses add to recent reports by providing age- and gender-adjusted estimates of the rate of decline in antibiotic utilisation for all antibiotics and broad-spectrum β-lactam antibiotics, for different prescribing indications and different population sub-groups defined by age and gender. The results show that the recent decline in AB utilisation is broadly based and has been observed in all sub-groups investigated. However, the decline in antibiotic utilisation has been at a faster rate for broad-spectrum β-lactam AB than all AB; the decline is consistent by gender but tended to be lower over age 55 years; the slowest rate of decline is observed for AB prescriptions with no coded indications. The results emphasise the utility of electronic health records for providing individual-patient data for surveillance of trends in antimicrobial utilisation and focusing future efforts at antimicrobial stewardship where these are most needed.

Contributors MG and XS conceived the study. XS analysed and interpreted the data, MG contributed additional analysis. XS wrote the first draft of the manuscript and both authors revised and approved the final draft. XS is the guarantor.

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Conflicts of Interest None

Data sharing statement CPRD data were analysed under licence and are not available for sharing.

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Table 1: Thirty most frequently used Read codes for 'other and non-specific' antibiotic prescribing indications.

Read Code	Read Term	Number of events[a]
9N31.00	Telephone encounter	51,504
6A...00	Patient reviewed	32,470
9N3A.00	Telephone triage encounter	26,900
246..00	O/E - blood pressure reading	25,502
242..00	O/E - pulse rate	15,918
9Z...00	Administration NOS	9,278
22A..00	O/E - weight	8,937
8CB..00	Had a chat to patient	8,191
9N1C.11	Home visit	7,813
1371	Never smoked tobacco	6,065
9....00	Administration	5,748
8CAL.00	Smoking cessation advice	5,664
8B3H.00	Medication requested	5,661
137S.00	Ex smoker	4,642
137P.00	Cigarette smoker	4,565
9N3G.00	SMS text message sent to patient	3,990
8B3S.00	Medication review	3,891
8CA..00	Patient given advice	3,838
246..11	O/E - BP reading	3,810
9N4..00	Failed encounter	3,514
661M.00	Clinical management plan agreed	3,305
9N58.00	Emergency appointment	2,930
1....00	History / symptoms	2,827
212..00	Patient examined	2,691
81H..00	Dressing of wound	2,543
9Na..00	Consultation	2,381
14L..00	H/O: drug allergy	2,277
1969	Abdominal pain	2,102
9N32.00	Third party encounter	1,948
679..11	Advice to patient - subject	1,939

[a]multiple codes per date were analysed

Table 2: Numbers of antibiotic prescriptions, and antibiotic prescribing rates, by year. Figures are frequencies except where indicated.

	2014	**2015**	**2016**	**2017**
General practices	102	102	102	102
Patients	1,025,539	1,058,805	1,069,513	1,071,293
Female (%)	520,336 (50.7)	536,082 (50.6)	542,051 (50.7)	543,324 (50.7)
Age (mean, sd, years)	39.4 (23.4)	39.5 (23.4)	39.7 (23.5)	39.9 (23.5)
Person-time (person years)	887,580	921,735	932,544	939,620
All AB prescriptions	539,219	494,185	482,917	459,476
All AB prescribing rate (per 1,000 person years)	608	536	518	489
Proportion of patients prescribed AB (%)	25.3	23.0	22.2	21.1
Mean number of AB prescriptions in patients prescribed	2.08	2.03	2.03	2.03
Broad-spectrum β-lactam AB prescriptions	195,750	174,353	167,056	153,423
Broad-spectrum β-lactam AB prescribing rate (per 1,000 person years)	221	189	179	163
Proportion of patients prescribed broad-spectrum β-lactam AB (%)	12.9	11.3	10.7	9.9
Mean number of broad-spectrum β-lactam AB prescriptions in patients prescribed	1.48	1.46	1.45	1.45

Table 3: Distribution of antibiotic prescriptions by broad groups of indications. Figures are frequencies except where indicated.

	2014		2015		2016		2017		Total	
	Freq.	%	Freq.	%	Freq.	%	Freq.	%	Freq.	%
AB prescriptions	539,219		494,185		482,917		459,476		1,975,797	
Respiratory conditions	168,852	31.3	146,025	29.5	140,263	29	129,032	28.1	584,172	29.6
Genito-urinary conditions	47,009	8.7	44,544	9	42,453	8.8	42,401	9.2	176,407	8.9
Skin conditions	39,579	7.3	35,299	7.1	33,640	7	32,003	7	140,521	7.1
Eye conditions	1,953	0.4	1,622	0.3	1,586	0.3	1,426	0.3	6,587	0.3
Non-specific codes	204,395	38	191,565	38.8	189,386	39.2	181,018	39.4	766,364	38.8
No medical codes	77,431	14.3	75,130	15.2	75,589	15.7	73,596	16	301,746	15.3

Table 4: Proportion of antibiotic prescriptions that were either acute or repeat prescriptions in 2017. Figures are frequencies (percent of row total).

	Total AB prescriptions	Acute	Repeat
AB prescriptions	459,476	381,310 (83)	78,166 (17)
Respiratory conditions	129,032	127,474 (99)	1,558 (1)
Genito-urinary conditions	42,401	41,740 (98)	661 (2)
Skin conditions	32,003	29,513 (92)	2,490 (8)
Eye conditions	1,426	1,399 (98)	27 (2)
Non-specific codes	181,018	163,804 (90)	17,214 (10)
No medical codes	73,596	17,380 (24)	56,216 (76)

Legend for Figure 1: Proportion of patients prescribed antibiotics in year by age-group and calendar year.

Legend for Figure 2: Forest plot showing annual relative reduction (95% confidence interval) in AB prescribing for all antibiotics and broad-spectrum β-lactam antibiotics between 2014 and 2017 for sub-groups of age and gender and different prescribing indications. Estimates were adjusted for age, gender and clustering by practice.

Legend for Figure 3: Bar chart showing changes from 2014 to 2017 in the proportion of antibiotic prescriptions for different antibiotic classes for males and females.